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Thirty-Four Months Control of Frail Patient with Multisystemic Affection Proved Erdheim Chester Disease: A Case Report

Emad Mohsen Barsoum[1], Fiby Samir Boules[1], May Gamal Ashour[2], Mohsen Samy Barsoum[1]

[1]Barsoum Oncology Center (BOC), Cairo, Egypt
[2]Radiation Oncology and Nuclear Medicine Department, National Cancer Institute, Cairo University, Cairo, Egypt
Email: emad_barsoum@hotmail.com, fiby.nader@yahoo.com, may.ashour@nci.cu.edu, eg.mbarsoum47@hotmail.com

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Abstract

Erdheim-Chester disease (ECD) is a rare non-Langerhans form of histiocytosis characterized by multisystemic involvement. We report a case of a 51-year-old male patient treated with pegylated IFN-α in a monthly schedule with low-dose prednisolone and achieved 34 months of control with minimal side effects.

Keywords

Erdheim-Chester Disease, Histiocytoses, Non-Langerhans Cell Histiocytoses

1. Introduction

Histiocytoses constitute a heterogeneous group of rare disorders, characterized by infiltration of myeloid cells to almost any organ with diverse macrophage or dendritic cell phenotypes. They are divided into Langerhans cells and non-Langerhans histiocytoses [1].

Non-Langerhans cell histiocytoses include numerous benign or malignant, localized or systemic, adult or pediatric diseases [2].

Some cases have an excellent prognosis after resection, and some even disappear spontaneously, but on the other hand, some progress rapidly and require intensive systemic therapies [2].

2. Case Presentation

We report a case of a 51-year-old male patient who presented in March 2018 with two months duration right loin pain radiating to the right lower limb not

responding to conservative treatment. The patient sought medical advice and underwent several investigations.

Computed tomography (CT) abdomen and pelvis showed lumbar vertebrae three body compression fracture, and wedge collapse suggests neoplastic infiltration, right sacral alum sclerotic marrow infiltration, and large retroperitoneal mass at right hypochondrial region.

PET-CT showed well defined large hepatic focal lesion measuring 15 × 10.5 × 12.2 cm with maximum standard uptake value (SUV max) 20.7, multiple small retroperitoneal, para-aortic and retrocaval lymph nodes largest measuring 2 × 2 cm, left para-aortic lymph node with SUV max 18.2, collapsed lumber vertebrae three associated with minimal prevertebral soft tissue mass SUV max 15.2, left symphysis pubis lytic lesion SUV max 17.6, right sacral ala sclerotic lesion SUV max 24.2 and right rib lesion SUV max 5.2.

CT-guided biopsy from the sacral and L3 vertebral lesion was done and proved histiocytic disorder like Erdheim-Chester disease, and after immunohistochemistry confirmed Erdheim -Chester disease, CD163 and CD 68 positive.

Serum protein electrophoresis showed polyclonal hypergammaglobulinemia.

The patient received palliative radiotherapy (3000 cGy/10 Fractions) to L3, and the sacrum ended in April 2018.

Then started pegylated interferon-alpha 160 mcg every 28 days with prednisolone 5 mg daily as the patient had poor performance status and couldn't tolerate the recommended weekly dose.

Two months later, in June 2018, the patient had an excellent clinical response in the form of pain improvement and regression of the metabolic activity of the lesions, so he was kept on the same treatment till October 2020, when PET CT showed mild progression in the form of mild increase of the metabolic activity of the old lesions and newly developed bony lesions.

So patient was offered to start chemotherapy adriamycin and vincristine, but he refused, so we advised him to continue pegylated interferon-alpha every 21 days instead of every 28 days.

Three months later, January 2021, PET CT showed stationary morphologic with metabolic regression of activity of large hepatic focal lesion 15 cm with SUV 15 versus 24.9, abdominal LNs largest left para-aortic 2 × 2 cm SUV 16.47 versus 28, numerous widespread bony lesions the most active at 4th rib SUV 15.9 versus 21, and left pubic lesion SUV 15.3 versus 21.65, so the patient was advised to continue same treatment with follow-up PET-CT every six months and BRAF V6000 gene mutation testing for evaluation for further treatment options.

3. Discussion

The first case of Erdheim-Chester disease (ECD) was documented in 1930 by Austrian doctor Jakob Erdheim and American pathologist William Chester [3]. Since then, there have been less than 1000 cases reported in the medical literature [4].

ECD is a non-Langerhans variant of histiocytosis that often manifests as multisystemic involvement in adults aged 40 - 60, with a male predominance [5].

Clinical signs range from asymptomatic to multisystemic life-threatening forms, including skeletal involvement, exophthalmos, diabetes insipidus, renal impairment, central nervous system, and/or cardiovascular involvement [5].

Prognosis differs according to disease burden and visceral involvement. Patients with visceral infiltration had a poorer prognosis than non-visceral infiltration. Arnaud *et al.* reported a 1-year survival rate of 96 percent and a 5-year survival rate of 68 percent [6]. Lung fibrosis is the leading cause of mortality, followed by renal failure due to retroperitoneal involvement and heart failure [7].

Treatment varies according to clinical presentation, symptoms, and disease burden. Patients with a low disease burden and asymptomatic may be kept without treatment with watchful waiting. Systemic corticosteroids, surgical excision, and local palliative radiotherapy may be used as symptomatic treatment but not as monotherapy, and other systemic therapy should be offered [8].

Surgical debulking is reserved for significant ocular lesions or intracranial lesions that are surgically resectable in ECD. Corticosteroids may be used immediately to alleviate edema, such as in cases of severe exophthalmos, or used as long-term palliation for patients who can't tolerate treatment side effects [8].

Malignant non-Langerhans cell histiocytoses have a poor prognosis in general, necessitating sophisticated treatment procedures with inconsistent outcomes. Before the discovery of IFN-α, several treatment regimens utilizing cytotoxic chemotherapies were described in small series, including vinca alkaloids, anthracyclines, methotrexate, and cyclophosphamide high-dose chemotherapy in combination with autologous stem cell transplantation [9] [10] [11].

PEG-IFN-α 135 μg SC/wk (standard dose) or 180 μg SC/wk (high dose) is ECD's gold standard of treatment as the first-line therapy with the most substantial clinical evidence. Case reports have shown a survival advantage for individuals with CNS or cardiac involvement when treated with any kind of IFN-α, particularly high-dose IFN-α [12] [13] [14] [15].

It was interesting to have a biomarker to target to improve results. Around 50% of patients with specific subtypes of non-Langerhans cell histiocytoses have BRAF mutations [2].

In November 2017, The FDA approved vemurafenib to treat selected adult patients with ECD who had the BRAF V6000 gene mutation [16].

Cobimetinib, a MEK inhibitor, has been utilized more recently in patients with BRAF wild-type cancer or who cannot tolerate or respond to Vemurafenib [17].

Other therapies include Tocilizumab, an anti-IL6 antibody now undergoing clinical trials in ECD patients based on systemic IL-6 elevations observed in ECD patients [18].

Sirolimus and prednisone were evaluated to disrupt immunological dysregulation in ECD. Additionally, the recent finding of an activating RAS mutation in ECD may give a reason for sirolimus suppression of mTOR in certain patients

[19].

Cladribine 6 mg/m^2 IV daily for five days every four weeks is a second-line therapeutic option. It has been used in clinical studies, although few published reports of its effectiveness [20] [21].

Imatinib 400 mg PO daily, even though no known mutations in KIT, ABL, or PDGFR are associated with histiocytic diseases. Specific histiocytic lesions in ECD and similar illnesses appear to display a high level of PDGFR-β. Imatinib treatment results in seven ECD individuals have been inconsistent, although it seems to be more beneficial in milder types of the condition [22] [23].

Infliximab 5 mg/mg IV every six weeks improved clinical outcomes in four individuals with refractory heart illness to IFN-α therapy [24].

4. Conclusions

ECD is a rare disease with emerging data about therapy. The only approved data about treatment is IFN-α weekly and anti BRAF for cases with BRAF V6000 gene mutation.

Unfortunately, all these treatment options have a lot of side effects and may not be suitable for frail patients with comorbidities.

The only accepted treatment for the frail patient was palliative radiotherapy and steroids. We used pegylated IFN-α with a monthly schedule with low-dose prednisolone to control this frail patient who didn't tolerate the approved weekly treatment as a palliative modality and achieved 34 months of control with minimal side effects.

We recommend tailoring treatment for patients with ECD to get adequate tumor control with minimal adverse events.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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